

REMARKS

Claims 13, 15 and 24-27 are pending. Claims 1-12, 14, 16-23 and 28-31 are canceled. No claims are herein amended.

In the Advisory Action mailed July 19, 2007, the Examiner has continued to find claims 15 and 24-27 allowable. Applicants express their gratitude.

I. Provisional Rejection over Appln. 09/854,568 has been Obviated

Applicants respectfully request the Examiner withdraw the provisional rejection of claim 13 for obviousness-type double patenting over claim 6 in co-pending U.S. Appln. Ser. No. 09/854,568 because claim 6 was canceled on June 26, 2007. The provisional rejection of claim 13 was apparently inadvertently maintained in the Advisory Action mailed July 19, 2007. A copy of the June 26, 2007 amendment canceling claim 6 was filed by Applicants in the above-captioned application in conjunction with their Interview Summary and Supplemental Response to Final Office Action filed June 26, 2007.

II. Specification Does Not Suggest Antibody of Claim 13 Inherent in Cited Art

The rejection of claim 13 for obviousness-type double patenting over U.S. Patent Nos. 4,298,590 and 4,486,538 (based on inherency) and for inherent anticipation over U.S. Patent No. 4,486,538 has been maintained. The Examiner alleges Applicants' specification admits an antibody to SEQ ID NO: 2 is inherent in the cited prior art or Applicants' specification admits an antibody to SEQ ID NO: 2 is an obvious variant inherently within the subject matter claimed in the cited prior patents. Applicants respectfully request the Examiner withdraw the rejection of claim 13 because Applicants' specification does not teach, suggest or imply antibodies to SEQ ID NO: 2 (or obvious variants thereof) were inherent in the cited prior art and Applicants' specification makes clear that antibodies to SEQ ID NO: 2 are a novel and nonobvious species of the genus of antimalignin antibodies.

Claim 13 is directed to a purified monoclonal antibody that specifically recognizes a peptide consisting of the amino acid sequence of SEQ ID NO: 2. SEQ ID NO: 2 is an epitope of the human oncoprotein known as malignin. Applicants have provided evidence in the record that the cited prior art does not inherently establish obviousness-type double patenting or anticipation of claim 13 because one of skill in the art would understand antimalignin antibodies disclosed in

the prior art were not necessarily directed at the SEQ ID NO: 2 epitope (as required for rejections under inherency). See MPEP § 2112. Applicants submitted three scientific papers in the above-captioned application on June 26, 2007 in support of the understanding of one of skill in the art: (1) Geysen, PNAS 81 (1994); (2) Earl, J. Virology, May (1994); and (3) Ditzel, J. Mol. Biol. 267 (1997). The Examiner nevertheless finds “it [] irrelevant what one of skill in the art expects” since “Applicants’ own specification states that raising antibodies to . . . SEQ ID NO: 2 results in production of antimalignin antibody . . .” July 19, 2007 Advisory Action at 3.

In support of the allegation that Applicants’ specification admits the antibody of claim 13 was inherent in the cited prior art, the Examiner provides the following citation from Applicants’ specification:

It has now been determined that the two longer sequences represent immunologic epitopes responsible for recognition by the body’s immune system and the resultant production *in vivo* of the specific antibody, anti-aglyco 10B (antimalignin antibody).

July 19, 2007 Advisory Action at 3 citing Appln. at 12, ll. 6-9. The Examiner concludes: “[I]t is irrelevant what one of skill in the art expects; inoculating an animal either with malignin or with SEQ ID NO: 2 produces antimalignin antibody, and said antibody has already been disclosed and patented in the prior art.” July 19, 2007 Advisory Action at 3. Applicants disagree.

Applicants respectfully traverse the Examiner’s allegations because (1) one of skill in the art would understand that Applicants’ references to the cited prior art do not admit that antibodies to SEQ ID NO: 2 had previously been produced, (2) any antibody alleged in the cited prior art that is produced *in vivo* does not meet each element of claim 13, which requires a “purified” and “monoclonal” antibody, and (3) the specification does not teach or suggest that the genus of antimalignin antibodies allegedly disclosed in the cited prior art were necessarily (inherently) directed to SEQ ID NO: 2.

1. One of skill in the art would understand Applicants did not admit prior production of antibody of claim 13

The Examiner has proposed that the cited prior art contains a description of antimalignin antibodies against intact malignin protein produced both clonally and *in vivo* and that Applicants’ several references to the cited prior art in their specification is an admission that

antibody to the specific SEQ ID NO: 2 epitope of malignin was inherently disclosed in the clonal and *in vivo* production of antimalignin antibody to the intact malignin protein. Applicants respectfully submit, however, that one of skill in the art would not consider Applicants' several references to the cited prior art to be such an admission. Because Applicants' references must be read in view of the understanding of one of skill in the art, Applicants will briefly recite the understanding of one of skill in the art as presented in Applicants' Supplemental Response after Final Office Action filed June 26, 2007. In that supplemental response, Applicants submitted (1) Geysen, PNAS 81 (1994); (2) Earl, J. Virology, May (1994); and (3) Ditzel, J. Mol. Biol. 267 (1997) for the proposition that one of skill in the art would not understand Applicants' references to the cited prior art to be an admission of inherent production of antibody against SEQ ID NO: 2.

Applicants respectfully submit the above-recited literature establishes the following understandings of one of skill in the art: (1) an intact *in vivo* protein such as malignin may contain several distinct epitopes against which antibodies to all epitopes would not be expected to be produced using the methods of the cited prior art; (2) each malignin epitope may have more than one antibody formed against it, none of which would necessarily be produced using the techniques of the cited art; (3) each antibody to a malignin epitope may have some (not complete) cross-affinity for another epitope, which is nevertheless unknown without further investigation; (4) knowing the specific amino acid sequence of any one of several epitopes provides the advantage of identifying a specific antibody to a specific epitope from among the genus of antibodies to any epitope on the intact protein (this advantage is seen in Applicants' disclosure concerning antibodies to synthetic SEQ ID NO:2); (5) absent specific disclosure of the specific sequence of SEQ ID NO: 2, it is not possible for one of skill in the art to necessarily produce an antibody to SEQ ID NO: 2 using only the intact malignin protein disclosed in the cited prior art.

In view of the foregoing understanding of one of skill in the art, the cited prior patents (wherein the SEQ ID NO: 2 epitope was not suggested or disclosed) did not necessarily disclose an antibody of claim 13. The Examiner has provided no evidence to refute this understanding.

As such, Applicants respectfully request the following discussion of Applicants' alleged admissions be considered from the unrefuted perspective of one of skill in the art.

2. Antibodies produced *in vivo* do not anticipate claim 13 and claim 13 is not an obvious variant of *in vivo* antibodies

In support of the Examiner's allegation that Applicants have admitted the necessary production of antibody to SEQ ID NO: 2 in the cited prior art, the Examiner quotes Applicants: "[SEQ ID NO: 2] represent[s] [an] immunologic epitope responsible for recognition by the body's immune system and the resultant production *in vivo* of the specific [antimalignin antibody]." July 19, 2007 Advisory Action at 3 citing Appln. at 12, lines 6-9. Using this quote, the Examiner suggests Applicants have admitted antibodies of claim 13 were inherently produced in the cited art. Applicants disagree.

The Examiner's reading of Applicants' statement is inappropriate because one of skill in the art would immediately recognize that Applicants' statement is directed to the *in vivo* production of antibodies to the malignin oncoprotein. The production of antibodies *in vivo*, as alleged by the Examiner, does not meet all the elements of claim 13, which requires a "purified" and "monoclonal" antibody. Further, the Examiner has provided no evidence that alleged production *in vivo* is an obvious variant of a "purified" and "monoclonal" antibody. The Examiner, therefore, has not made a *prima facie* showing that Applicants admit the inherent disclosure of antibodies meeting all of the elements of claim 13. Applicants respectfully traverse the Examiner's allegation on this first ground and request withdrawal of the rejection of claim 13.

3. Cited art does not inherently contain antibody of claim 13

The Examiner's allegation that Applicants' have admitted inherent disclosure of antibodies to SEQ ID NO: 2 is further inappropriate because one of skill in the art would immediately recognize Applicants' statement to be directed to the production of the genus of any antibody against any epitope on the entire malignin oncoprotein for the purpose of establishing that native aglyco substances are in fact responsible for the immune response observed in human cancer and not for the purpose of establishing that antibodies to SEQ ID NO: 2 were present in the prior art. Appln. at 12 (antimalignin antibody is "tested by the standard immunoabsorption technique using immobilized intact aglyco 10B" for the purpose of "establishing rigorously that

the native biological aglyco substances are in fact responsible for the immune response discovered in human cancer.”)

One of skill in the art would further understand based on the standard immunoabsorption technique used by Applicants that “the specific antimalignin antibody” referenced in the Examiner’s quotation is the genus of antimalignin antibodies to intact malignin oncoprotein.

Applicants state:

These synthetic peptides have been injected into animals, and these animals produced the specific antimalignin antibody anti-aglyco 10B as tested by the standard immunoabsorption technique using immobilized intact aglyco 10B.

Appln. at 12 (emphasis added). One of skill in the art would immediately recognize that the standard immunoabsorption technique described by Applicants would result in identifying the genus of any antibody that bound to any portion of the intact malignin protein and would not be effective in identifying a species of antimalignin antibody against a particular epitope.

The Examiner, nevertheless, incorrectly presumes that Applicants’ reference to “the specific antibody” in Applicants statement admits prior disclosure of a species of antibody directed to a single epitope. This presumption cannot be true even upon initial review of Applicants’ statement because the statement itself references two different antibodies directed to two different epitopes that are expressly differentiated by Applicants. *See, e.g.*, Appln. at 25 (“In contrast to the results obtained with [SEQ ID NO: 2], for [SEQ ID NO: 1] the post-injection levels of IgG rose to a very high level.”)

Further, upon reading the entire paragraph from which the Examiner has drawn Applicants’ quote, one of skill in the art would understand that Applicants’ comments were directed to providing that aglyco 10B (malignin) is the antigen responsible for the antimalignin antibody immune system response observed in cancer:

These synthetic peptides, when injected into an animal, induce the production of elevated concentrations of antimalignin antibody, thus establishing rigorously that the native biological aglyco substances are in fact responsible for the immune response discovered in human cancer.

Appln. at 12. One of skill in the art would understand Applicants’ comments were not directed to demonstrating that SEQ ID NO:2 was the antigen responsible for the immune response in

cancer but that native biological aglyco 10B was the responsible antigen and SEQ ID NO: 2 is an epitope on aglyco 10B. The Examiner has not read Applicants' statements in context and has erroneously alleged Applicants' admission of inherent production of the antibody of claim 13.

Throughout the specification, Applicants make clear that SEQ ID NO: 2 is an epitope of malignin that produces a species of antimalignin antibody. *See* Appln. at 12. Applicants in no way limit the number of antimalignin antibody species to the two expressly disclosed species. Applicants state: "[T]he two longer sequences represent immunologic epitopes responsible for recognition by the body's immune system and the resultant production *in vivo* of the specific antibody, anti-aglyco 10B (antimalignin antibody)." *Id.* One of skill in the art would understand from the word "represent" and absence of the article "the" before the word "epitope" that Applicants were not limiting the genus of antimalignin antibody to antibodies against SEQ ID NO: 1 and SEQ ID NO: 2. Further, as established by Geysen (1994), Earl (1994), and Ditzel (1997), one of skill in the art would have no doubt that more epitopes on the malignin protein may be located with implementation of additional research techniques. *See, e.g.*, Ditzel at 691 ("[To] obtain antibodies to a range of epitopes[,] may require more than simple selection of the library against the antigen of interest." Instead, one may use a set of "selection procedures leading to the isolation of an extended set of specificities to a single antigen.").

4. Alleged disclosure of the genus of antimalignin antibodies is not *prima facie* support for inherency

The Examiner's allegation, therefore, does not rise to the level of *prima facie* support for inherent anticipation or obviousness-type double patenting based on inherency. *See* MPEP § 2112(IV). Disclosure of a genus is not inherent disclosure of a species: "A prior art reference that discloses a genus still does not inherently disclose all species within that broad category but must be examined to see if a disclosure of the claimed species has been made or whether the prior art reference merely invites further experimentation to find the species." *Id.* quoting and explaining *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1367 (Fed. Cir. 2004) (emphasis added). Because Applicants do not admit in the specification that the species of antibody against SEQ ID NO: 2 is inherently disclosed in the cited prior art, Applicants respectfully request the Examiner withdraw the rejection of claim 13 on this second ground.

5. Example 6 teaches “antimalignin antibodies” are a genus

In the February 7, 2007 Final Office Action in the above-captioned application, the Examiner has alleged Applicants’ discussion in Example 6 of evidence that SEQ ID NO: 1 and SEQ ID NO: 2 are epitopes on the malignin oncoprotein is an admission of inherent disclosure of an antibody against SEQ ID NO: 2 in the cited prior art. *See id.* at 10-11. As discussed above, however, Applicants’ specification consistently refers to antimalignin antibodies as the genus of antibodies that bind any epitope on the intact malignin protein and Applicants’ discussion in Example 6 is not different.

For example, the initial sub-heading of Example 6 on page 23 asserts that Example 6 establishes “Proof that the Peptide Sequences Determined in Aglyco 10B are True Epitopes for the Production of Antimalignin Antibody.” As such, one of skill in the art would understand Applicants’ data was directed to demonstrating SEQ ID NO: 1 and SEQ ID NO: 2 were epitopes of malignin. One of skill in the art would not understand Applicants’ data to be directed to proving that all antimalignin antibodies of the genus are in fact the same species. Instead, the skilled artisan would immediately understand that different antibodies are necessarily produced to different epitopes. *See, e.g.*, Geysen at 3999, right column (noting that the data “highlight the variability possible in the antibody composition between sera [of different animals]”).

In Example 6, Applicants disclose that an increase in F-TAG concentration preceded an increase in S-TAG concentration in both *in vitro* isolated lymphocytes challenged with intact malignin (also called aglyco 10B) and *in vivo* tests with SEQ ID NO:1 and SEQ ID NO:2. Appln. at 23. Applicants then explain: “The repetition of this phenomenon with synthetic peptide epitopes injected into rabbits is further confirmation of the fact that the synthetic peptides reproduce exactly the production and release into serum of antimalignin antibody.” *Id.* at 23-24. The Examiner alleges that in this quote, Applicants have admitted prior production of antibody to SEQ ID NO: 2. Applicants respectfully disagree.

The Examiner’s allegation again takes Applicants’ statement out of context. Applicants have not stated that the synthetic peptides reproduce the same species of antimalignin antibody as the intact malignin. First, as established above, it cannot be true that Applicants teach the synthetic peptides reproduce the exact same antimalignin antibody as intact malignin because

Applicants expressly teach SEQ ID NO: 1 and SEQ ID NO: 2 produce expressly different antibodies. *See* Appln. at 25. Next, Example 6 is expressly provided as evidence that SEQ ID NO: 1 and SEQ ID NO: 2 are epitopes on the intact malignin protein as opposed to evidence that SEQ ID NO: 2 is an epitope on the intact malignin protein to which an antibody necessarily was produced. Finally, Applicants' statement makes clear to one of skill in the art that the phenomenon Applicants are discussing is the rate of "production and release into serum" of the genus of antimalignin antibodies, not the exactness of a species of antibody directed to a particular epitope. Applicants' language itself, therefore, belies the Examiner's allegation that Applicants admit all species of antimalignin antibodies are exactly the same.

Because Applicants' discussion of the rate of production and release into serum of the genus of antimalignin antibody makes clear that Applicants considered antimalignin antibody to be a genus, Applicants respectfully request the Examiner withdraw the allegation that Applicants admit an antibody directed specifically to SEQ ID NO: 2 is inherently disclosed in the cited prior art. Applicants respectfully request the Examiner withdraw the rejection of claim 13 based on this third ground.

III. Request for Examiner Interview if Interview Deemed Helpful

In view of the foregoing arguments, Applicants respectfully believe the application is in condition for allowance of all claims. The Examiner has found claims 15 and 24-27 allowable, for which Applicants express their gratitude. Applicants additionally respectfully submit the reasons for rejection of claim 13 have been narrowed to the discreet issue of inherent anticipation and inherent obviousness-type double patenting based on the allegation of an admission in Applicants' specification. Should the Examiner determine that a personal interview would be helpful in considering Applicants' arguments on this single remaining issue, Applicants respectfully request such an interview with Examiner Emch and Supervisory Examiner Andres. Applicants invite the Examiner to contact the undersigned at the Examiner's convenience should the Examiner wish to discuss the possibility of an interview.

CONCLUSION

It is believed that the present claims are in conditions for allowance and Applicants earnestly request the same. Extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a). The fee for a Request for Continued Examination, the fee for the three-month extension of time and any other fee that the Commissioner determines necessary for entry of the instant paper are hereby authorized to be charged to Kenyon & Kenyon LLP Deposit Account No. 11-0600.

The Examiner is invited to contact the undersigned attorney if necessary to expedite allowance. An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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